Clinical trial results:
A Double-blind, Randomized, Placebo-controlled, Multicentre, Relapse-prevention Study of Vortioxetine in Paediatric Patients Aged 7 to 11 Years With Major Depressive Disorder

Summary

EudraCT number	2010-020493-42
Trial protocol	BG PL LV ES
Global end of trial date	28 April 2022

Results information

Result version number	v2 (current)
This version publication date	25 January 2023
First version publication date	04 October 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	13546A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05014919
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark, 2500
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S, +45 36301311, LundbeckClinicalTrials@lundbeck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000455-PIP02-10
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2022
Global end of trial reached?	Yes
Global end of trial date	28 April 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trail was to evaluate the efficacy of vortioxetine in the prevention of relapse of major depressive episodes in paediatric participants with Major Depressive Disorder (MDD).

Protection of trial subjects:

This study was conducted in compliance with Good Clinical Practice.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 6
Country: Number of subjects enrolled	Mexico: 14
Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Ukraine: 1
Worldwide total number of subjects	35
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	29
Adolescents (12-17 years)	6

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study population included de novo participants as well as rollover participants from other paediatric vortioxetine studies (Studies 12709A [NCT02709655] and 12712A [NCT02871297]) who, in the investigator's opinion, would benefit from continued treatment with vortioxetine.

Pre-assignment

Screening details:

Rollover participants from Study 12709A enrolled to the open-label period and rollover participants from Study 12712A randomized to double-blind period. Overall 35 participants treated in this study: 33 in open-label period (24 de novo and 9 rollover participants from Study 12709A) and 4 in double-blind period (2 rolled-over from Study 12712A).

Period 1

Period 1 title	Open-Label (12 Weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Open-Label Treatment: Vortioxetine

Arm description:

Participants initiated treatment with vortioxetine tablets 5 milligrams (mg)/day orally for the first 2 days and thereafter they received 10 mg/day vortioxetine. Based on the response and dose-limiting adverse events (AEs), vortioxetine dose could be up- or down-titrated with 5 mg/day to a maximum of 20 mg/day during the first 8 weeks. From Week 8 to Week 12, the dose remained fixed.

Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Vortioxetine was administered per dose and schedule specified in the arm description.

Number of subjects in period 1[1]	Open-Label Treatment: Vortioxetine
Started	33
Received at least 1 dose of study drug	33
Completed	5
Not completed	28
Consent withdrawn by subject	2
Based on Results From Vortioxetine Study	15
Adverse event, non-fatal	1
Sponsor Decision	4
Study Terminated by Sponsor	5

Lack of efficacy	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 35 participants enrolled in this study: 33 in the open-label period and 2 in the double-blind period.

Period 2

Period 2 title	Double-Blind (26 Weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-Blind Relapse Prevention: Vortioxetine

Arm description:

Participants continued on the same fixed dose of vortioxetine as during the end of the open-label period for 26 weeks in the double-blind relapse prevention period.

Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Vortioxetine was administered per dose and schedule specified in the arm description.

Arm title	Double-Blind Relapse Prevention: Placebo

Arm description:

Participants received placebo for 26 weeks in the double-blind relapse prevention period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to vortioxetine was administered per schedule specified in the arm description.

Number of subjects in period 2[2]	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo
Started	2	2
Received at least 1 dose of study drug	2	2
Completed	1	0
Not completed	1	2
Based on Results From Vortioxetine Study	1	1
Study Terminated by Sponsor	-	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Of 5 participants who completed open-label period, only 2 participants entered in the double-blind period.

Baseline characteristics

Reporting groups

Reporting group title	Open-Label Treatment: Vortioxetine

Reporting group description:

Participants initiated treatment with vortioxetine tablets 5 milligrams (mg)/day orally for the first 2 days and thereafter they received 10 mg/day vortioxetine. Based on the response and dose-limiting adverse events (AEs), vortioxetine dose could be up- or down-titrated with 5 mg/day to a maximum of 20 mg/day during the first 8 weeks. From Week 8 to Week 12, the dose remained fixed.

Reporting group values	Open-Label Treatment: Vortioxetine	Total	
Number of subjects	33	33	
Age Categorical Units: Subjects			
Children (2-11 years)	27	27	
Adolescents (12-17 years)	6	6	
Gender Categorical Units: Subjects			
Female	18	18	
Male	15	15	
Ethnicity Units: Subjects			
Hispanic or Latino	18	18	
Not Hispanic or Latino	15	15	
Unknown or Not Reported	0	0	
Race Units: Subjects			
White	13	13	
Black or African American	3	3	
Asian	1	1	
Other	16	16	

Subject analysis sets

Subject analysis set title	Double-Blind Relapse Prevention: Vortioxetine
Subject analysis set type	Full analysis

Subject analysis set description:

Participants continued on the same fixed dose of vortioxetine as during the end of the open-label period for 26 weeks in the double-blind relapse prevention period.

Subject analysis set title	Double-Blind Relapse Prevention: Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received placebo for 26 weeks in the double-blind relapse prevention period.

Reporting group values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo	
Number of subjects	2	2	

Age Categorical Units: Subjects			
Children (2-11 years)	2	2	
Adolescents (12-17 years)	0	0	
Gender Categorical Units: Subjects			
Female	1	1	
Male	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	2	1	
Not Hispanic or Latino	0	0	
Unknown or Not Reported	0	1	
Race Units: Subjects			
White	0	2	
Black or African American	0	0	
Asian	0	0	
Other	2	0	

End points

End points reporting groups

Reporting group title	Open-Label Treatment: Vortioxetine
Reporting group description:	
Participants initiated treatment with vortioxetine tablets 5 milligrams (mg)/day orally for the first 2 days and thereafter they received 10 mg/day vortioxetine. Based on the response and dose-limiting adverse events (AEs), vortioxetine dose could be up- or down-titrated with 5 mg/day to a maximum of 20 mg/day during the first 8 weeks. From Week 8 to Week 12, the dose remained fixed.	
Reporting group title	Double-Blind Relapse Prevention: Vortioxetine
Reporting group description:	
Participants continued on the same fixed dose of vortioxetine as during the end of the open-label period for 26 weeks in the double-blind relapse prevention period.	
Reporting group title	Double-Blind Relapse Prevention: Placebo
Reporting group description:	
Participants received placebo for 26 weeks in the double-blind relapse prevention period.	
Subject analysis set title	Double-Blind Relapse Prevention: Vortioxetine
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants continued on the same fixed dose of vortioxetine as during the end of the open-label period for 26 weeks in the double-blind relapse prevention period.	
Subject analysis set title	Double-Blind Relapse Prevention: Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received placebo for 26 weeks in the double-blind relapse prevention period.	

Primary: Time to Relapse in the Double-blind Period

End point title	Time to Relapse in the Double-blind Period[1]
End point description:	
Relapse was defined as either a total score ≥40 on the Children Depression Rating Scale Revised Version (CDRS-R) with a history of 2 weeks of clinical deterioration, or clinical deterioration as judged by the clinician. The CDRS-R is rated by a clinician following interviews with the child and parent and consists of 17 items out of which 3 items rate nonverbal observations (listless speech, hypoactivity, and depressed affect). Fourteen items are rated on a 7-point scale from 1 to 7, and 3 items (sleep disturbance, appetite disturbance, and listless speech) are scored on a 5-point scale from 1 to 5. A rating of 1 indicates normal functioning and a higher number indicates a greater degree of depression. The total score ranges from 17 (normal) to 113 (severe depression). Due to the early termination of study and limited number of participants who completed the double-blind period, the efficacy analyses were not performed and data were not collected for this endpoint.	
End point type	Primary
End point timeframe:	
From randomisation to Week 26 in the double-blind treatment period	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint is for double-blind period only.

End point values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: weeks				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - The efficacy analyses were not performed and data were not collected for this endpoint.

[3] - The efficacy analyses were not performed and data were not collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse Rate in the Double-blind Period: Percentage of Participants With Relapse

End point title	Relapse Rate in the Double-blind Period: Percentage of Participants With Relapse

End point description:

Relapse was defined as either a total score ≥40 on the CDRS-R with a history of 2 weeks of clinical deterioration, or clinical deterioration as judged by the clinician. The CDRS-R is rated by a clinician following interviews with the child and parent and consists of 17 items out of which 3 items rate nonverbal observations (listless speech, hypoactivity, and depressed affect). Fourteen items are rated on a 7-point scale from 1 to 7, and 3 items (sleep disturbance, appetite disturbance, and listless speech) are scored on a 5-point scale from 1 to 5. A rating of 1 indicates normal functioning and a higher number indicates a greater degree of depression. The total score ranges from 17 (normal) to 113 (severe depression). Due to the early termination of study and limited number of participants who completed the double-blind period, the efficacy analyses were not performed and data were not collected for this endpoint.

End point type	Secondary

End point timeframe:

From randomisation to Week 26 in the double-blind treatment period

End point values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: percentage of participants				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - The efficacy analyses were not performed and data were not collected for this endpoint.

[5] - The efficacy analyses were not performed and data were not collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Children's Depression Rating Scale - Revised Version (CDRS-R) Total Score at Week 26

End point title	Change From Baseline in Children's Depression Rating Scale - Revised Version (CDRS-R) Total Score at Week 26

End point description:

The CDRS-R is a clinician-rated scale to measure the severity of depression in children and adolescents. The CDRS-R is rated by a clinician following interviews with the child and parent and consists of 17 items out of which 3 items rate nonverbal observations (listless speech, hypoactivity, and depressed affect). Fourteen items are rated on a 7-point scale from 1 to 7, and 3 items (sleep disturbance,

appetite disturbance, and listless speech) are scored on a 5-point scale from 1 to 5. A rating of 1 indicates normal functioning and a higher number indicates a greater degree of depression. The total score ranges from 17 (normal) to 113 (severe depression). Due to the early termination of study and limited number of participants who completed the double-blind period, the efficacy analyses were not performed and data were not collected for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - The efficacy analyses were not performed and data were not collected for this endpoint.

[7] - The efficacy analyses were not performed and data were not collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Global Impression - Severity of Illness (CGI-S) Score at Week 26

End point title	Change From Baseline in Clinical Global Impression - Severity of Illness (CGI-S) Score at Week 26

End point description:

The CGI-S provides the clinician’s impression of the participant’s current state of mental illness. The clinician uses his or her clinical experience of this participant population to rate the severity of the participant’s current mental illness on a 7-point scale ranging from 1 (normal – not at all ill) to 7 (among the most extremely ill participants). Due to the early termination of study and limited number of participants who completed the double-blind period, the efficacy analyses were not performed and data were not collected for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[8] - The efficacy analyses were not performed and data were not collected for this endpoint.

[9] - The efficacy analyses were not performed and data were not collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression - Global Improvement (CGI-I) Score at Week 26

End point title	Clinical Global Impression - Global Improvement (CGI-I) Score at Week 26

End point description:

The CGI-I provides the clinician's impression of the participant's improvement (or worsening). The clinician assesses the participant's condition relative to a baseline on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). Due to the early termination of study and limited number of participants who completed the double-blind period, the efficacy analyses were not performed and data were not collected for this endpoint.

End point type	Secondary

End point timeframe:

Week 26

End point values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[10] - The efficacy analyses were not performed and data were not collected for this endpoint.

[11] - The efficacy analyses were not performed and data were not collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Paediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) Total Score (Items 1 to 14) at Week 26

End point title	Change From Baseline in Paediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) Total Score (Items 1 to 14) at Week 26

End point description:

The PQ-LES-Q is a participant-rated scale designed to assess satisfaction with life. It is an adaptation of the Quality of Life Enjoyment and Satisfaction Questionnaire, which is used to measure quality of life in adults. The PQ-LES-Q consist of 15 items, item 1 to 14 assess the degree of satisfaction experienced by participants in various areas of daily functioning, and item 15 allows participants to summarise their experience in a global rating. Each item is rated on a 5-point scale from 1 (very poor) to 5 (very good). The total score range of item 1 to 14 is 14 to 70, with higher scores indicating greater satisfaction. Due to the early termination of study and limited number of participants who completed the double-blind period, the efficacy analyses were not performed and data were not collected for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[12] - The efficacy analyses were not performed and data were not collected for this endpoint.

[13] - The efficacy analyses were not performed and data were not collected for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Vortioxetine

End point title	Plasma Concentration of Vortioxetine

End point description:

Due to early termination of the study, the pharmacokinetic analyses were not performed and the data were not collected.

End point type	Secondary

End point timeframe:

From randomisation to Week 26 in the double-blind treatment period

End point values	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: nanograms (ng)/milliliter (mL)				
arithmetic mean (standard deviation)	()	()		

Notes:

[14] - Pharmacokinetic analyses were not performed and the data were not collected.

[15] - Pharmacokinetic analyses were not performed and the data were not collected.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Week 0) up to Week 42

Adverse event reporting additional description:

All-patients-enrolled (APES) included all participants enrolled to the 12-week open-label, flexible-dose treatment period who took at least 1 dose of study drug. All-patients-randomized set (APRS) included all participants randomized to the 26-week double-blind treatment period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Open-Label Treatment: Vortioxetine

Reporting group description:

Participants initiated treatment with vortioxetine tablets 5 mg/day orally for the first 2 days and thereafter they received 10 mg/day vortioxetine. Based on the response and dose-limiting AEs, vortioxetine dose could be up- or down-titrated with 5 mg/day to a maximum of 20 mg/day during the first 8 weeks. From Week 8 to Week 12, the dose remained fixed.

Reporting group title	Double-Blind Relapse Prevention: Vortioxetine

Reporting group description:

Participants continued on the same fixed dose of vortioxetine as during the end of the open-label period for 26 weeks in the double-blind relapse prevention period.

Reporting group title	Double-Blind Relapse Prevention: Placebo

Reporting group description:

Participants received placebo for 26 weeks in the double-blind relapse prevention period.

Serious adverse events	Open-Label Treatment: Vortioxetine	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Open-Label Treatment: Vortioxetine	Double-Blind Relapse Prevention: Vortioxetine	Double-Blind Relapse Prevention: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 33 (24.24%)	0 / 2 (0.00%)	1 / 2 (50.00%)
Investigations			

Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 33 (3.03%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 33 (3.03%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 33 (3.03%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Food poisoning			
subjects affected / exposed	1 / 33 (3.03%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	6 / 33 (18.18%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	7	0	0
Vomiting			
subjects affected / exposed	2 / 33 (6.06%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Coronavirus infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 33 (3.03%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 33 (0.00%)	0 / 2 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated based on new efficacy data from another study. The main primary and secondary efficacy objectives were not assessed due to termination of the study and the limited number of participants who completed the double-blind period.

Notes: